Information Mastery: Maximizing Usefulness from Review Articles

CDR Ken Yew
Bureau of Medicine and Surgery
NEHC EBHC Workshop

Slides adapted and modified with permission from University of Virginia Information Mastery Course with additional slides by A. J. Viera, M.D.

Objectives

- Describe types of review articles
- Introduce Systematic Reviews
- Determine the validity of a systematic review
- Large group exercise – Reading a systematic review article

The Where: The Flora and Fauna of the Medical Jungle

- Original Research
- Academic Reviews
- Practice Guidelines
- Decision/Cost Analysis
- Translation Journals
- Continuing Medical Education
- Clinical Experience
- Experts
- Newsletters and Survey Services
- Pharmaceutical Representatives
- Computer sources
- Audiotapes
- Patients/Qualitative Research

The Usefulness Equation

Usefulness of any source = Relevance x Validity / Work

Two Types of Information

- ***Background Questions***
  - **Students**
  - **“What is…?”**
  - **Normal phys. & pathophysiology**

- ***Foreground Questions***
  - **Experienced clinicians**
  - **Managing patients**
  - **Specific problems**
  - **Diagnosis (tests), prognosis, treatment options**

Medical Literature

- Original Research
  - Analytic, primary studies
    - Case-control studies
    - RCTs
- Summaries from original research
  - Integrative, secondary studies
    - Nonsystematic reviews
    - Systematic reviews

Types of Reviews

- Text books

- "Academic reviews"
  - Summary type
  - Synthesi

Textbooks

- Collection of review articles
- **Work:** generally low
- **Relevance:** variable, often not POEM focused
- **Validity:** variable
  - Long lag time to publish
  - Long list of references, but…
  - Conclusions often not linked to supporting evidence
- Most useful for reviewing prior knowledge (**retracing**)
  - background questions
  - less for seeking answers to new questions (**hunting**)

Summary-type Review

- "Broadly paint landscape"
- Variably cite/use evidence
  - AFP Articles, "throw-away" journals
  - Expertise of author varies inversely with quality of review- Oxman/Guyatt
  - Often begin with conclusions and find supporting references
  - References may be inaccurate, out of date, or disease-oriented

Usefulness of summary reviews

- **Work:** seemingly low
  - One-stop shopping?
  - Confirming relevance and validity increases work
- **Relevance:** variable
  - Often not POEM-focused
- **Validity:** variable
  - Lack of “methods” limits critical appraisal
- Most useful for **retracing or foraging**
  - If find a common POEM, need to find original reference to validate

Buyer Beware!

“Unsystematic reviews lead to unsystematic conclusions. Readers looking for a shortcut to understanding evidence about health problems and patient care should at least look for reviews by those who have not taken shortcuts”

What we're looking for...

"The review article itself should be the product of scientific investigation in which the participants are original investigations (research) rather than patients."

Synthesis Reviews

- **Systematic reviews = original research**
  - **Answer one or two specific questions**
  - **Review primary literature with strict criteria for inclusion**
  - **Evaluate the evidence included**
  - **Summarize the data to draw (new) conclusions**
- **Meta-analysis**
  - **Subset of SR's, when data can be mathematically combined**
  - **Achieve power not possible by single study**

Usefulness of Synthesis Reviews

- **Work:** potentially low
  - Summarizes all data on single question in one place
  - Cochrane Library
- **Relevance:** variable
  - Often mix of POEMs and DOEs
  - Scan outcome list to decide
- **Validity:** evaluate-able as is
  - Worksheet review
- Useful for **hunting and foraging**

Potential Benefits of Meta-Analysis

- Increase # of subjects →improves statistical power to detect differences
- Provide more objective appraisal when studies disagree
- Improve estimates of effect size or magnitude of association
- Address questions not posed at start of individual trials
- Assimilate large amounts of information
- Improve quality of primary research

e.g., Benefits of Meta-Analysis

- **Too small a sample in an RCT may not detect difference even though one exists (type II error)**
- **Review of RCTs* with negative results 1975 to 1990 in JAMA, Lancet, NEJM: majority had too few patients**
  - **Insufficient power to detect 25% to 50% difference**

* Moher D, Dulberg CS, Wells GA. Statistical power, sample sized, and their reporting in randomized controlled trials. JAMA 1994: 272:122-4.

Meta-analysis

- **Only as good as the research on which it is based!**

- **Magnesium, myocardial infarction, meta-analysis and megatrials. Drug Ther Bull 1995;33:25-7.**
  - **Giving IV Mg++ beneficial to MI patients**
- **ISIS-4 (58,000 patients) = no benefit**
- **Meta-analysis misleading b/c of publication bias and methodologic weaknesses in smaller trials**

Threats to Validity of Meta-analysis

- Combining studies that are dissimilar
- Publication bias
- Including poor-quality studies

Determining the usefulness of reviews

Let’s look at the worksheets

Two main steps

- Determine *Relevance*
- Determine *Validity*

Reviews: Determining Relevance

A. Addressing specific clinical question?

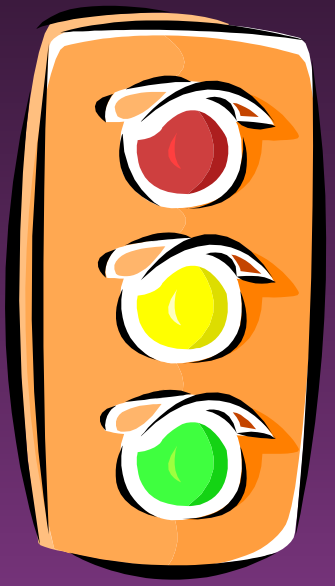
   Patient-oriented evidence?

B. Common problem?

C. Change your practice?

Reviews: Determining Validity

- Answer ALL worksheet questions
- Stop = “fatal flaw”
  - *Caution* perhaps better word
  - Any “no’s” need explanation and guesstimate as to how the flaw affects the study results



Worksheet Qs: Finding the studies

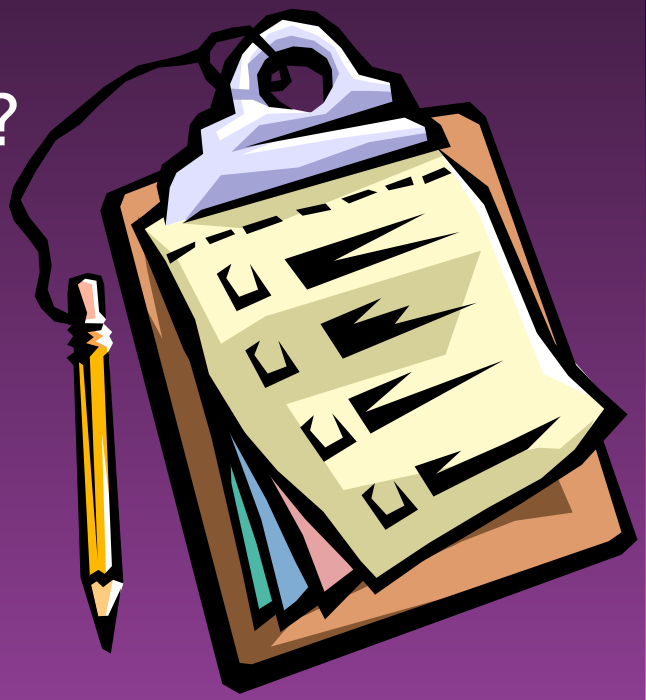
- Clearly stated?
  - Terms appropriate? MESH-linked? None missing?
- Comprehensive?
  - Medline + another
    - MEDLINE misses >50% of articles
    - CCTR is especially good source
  - Bibliographic review
  - Unpublished literature
    - conference abstracts, personal correspondence with important investigators or pharmaceutical companies, grey literature
- Done by more than one person and compared

Worksheet Qs: Selecting the studies

- *A priori* inclusion criteria
- Criteria
  - Minimum factors: Population/problem; intervention/comparison; outcomes; study design
  - Prefer no language restriction (“Tower of Babel” bias)
  - Sometimes validity criteria incorporated
- Best if done independently by 2 investigators
  - Possibly blinded to author/journal/study results

Worksheet Qs: Validity of included studies

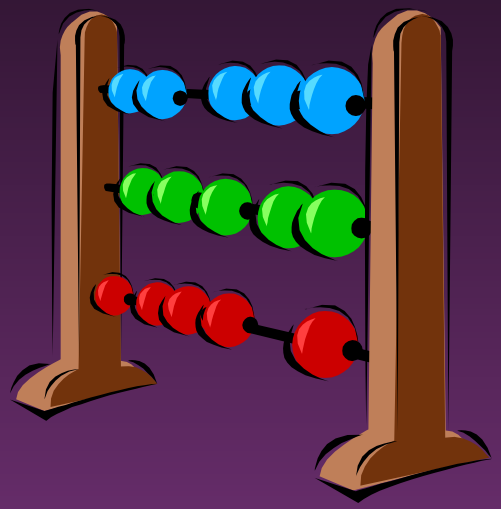
- Appropriate criteria?
  - Assurance that criteria specific to type of article employed (therapy, diagnosis, prognosis, etc)
  - If therapy: randomization, blinding, concealed allocation, follow-up
- Process independent by ≥ 2 authors?
  - Surprising differences!
  - Why blinding may be important:
    - 2 sample articles, same study methods
    - One finds benefit, other does not
    - “serious flaws” in article without benefit



Worksheet Qs: Validity

- Were the included studies valid?
  - Garbage in = garbage out
  - If yes, no problem
  - If no, how did authors handle this?
    - Exclusion criteria
    - Subanalysis with comparison of results
    - Need to consider how these flaws effect results/conclusions

Worksheet Qs: Analyzing the data



- Statistical homogeneity
  - Based on numerical results & CIs
  - Higher p values, less heterogeneous
  - If NOT homogeneous?
    - Random effects model instead of fixed effects
    - Need qualitative explanation

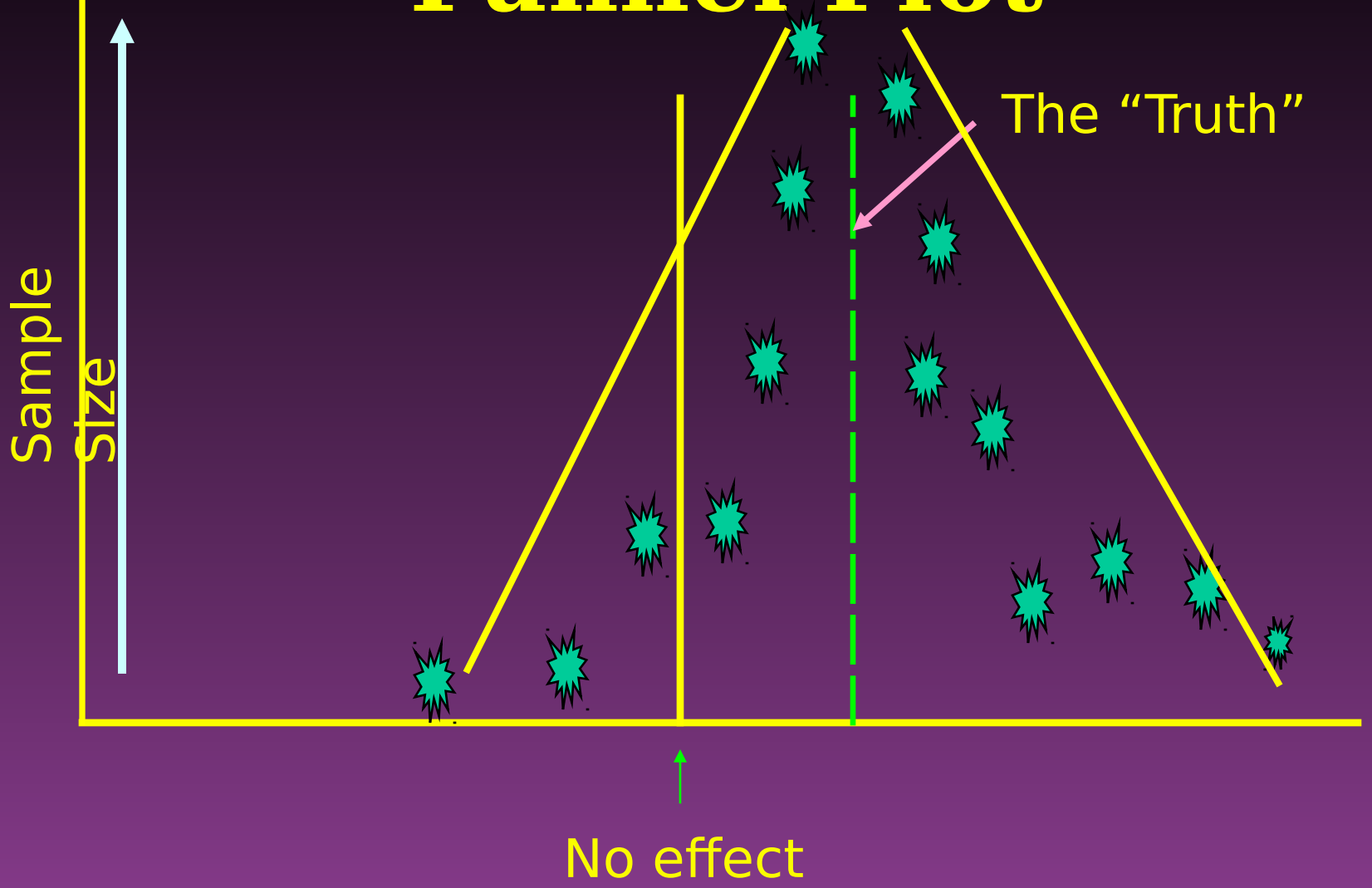
Worksheet Qs: Analyzing the data

- Appropriateness of combining data?
  - Qualitative homogeneity = your gestalt
  - Consider factors of population, interventions, outcomes (and methods to measure), design
- Publication bias
  - Small, negative trials less likely to be published
  - Have all the relevant studies been identified?
  - Examined by funnel plot

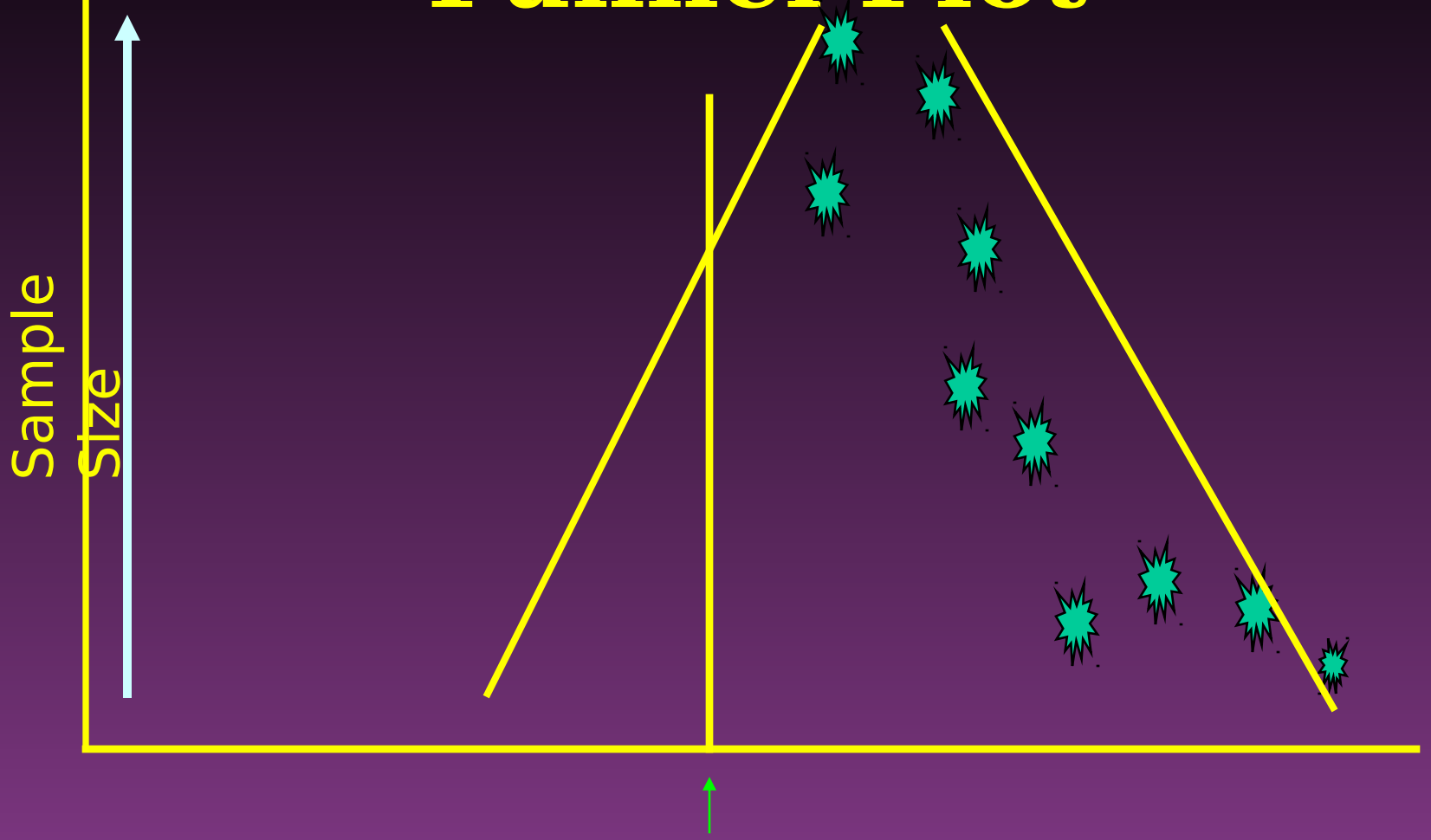
Funnel Plot

- Used to assess presence and extent of possible publication bias
- Smaller studies, by chance alone, expected to produce results with greater variation
- Should look like a funnel
- Incomplete lower funnel suggests missing studies

Funnel Plot

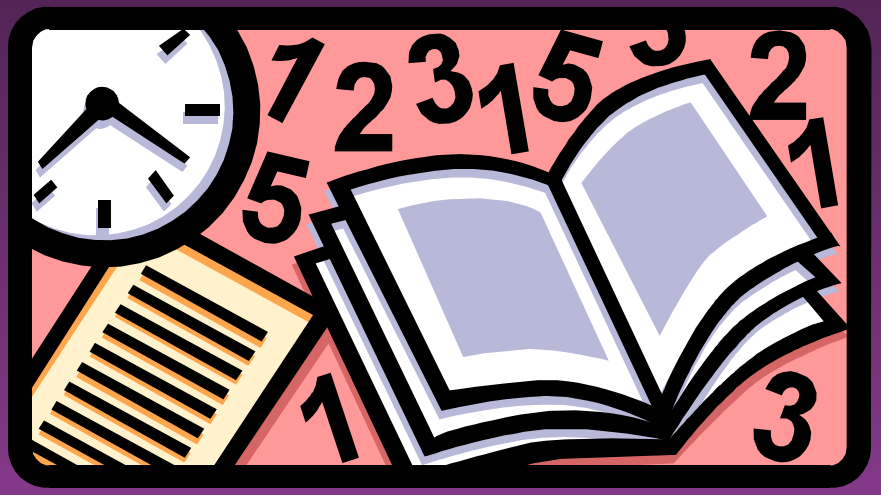


Funnel Plot



Worksheet Qs: Interpreting the data

- Statistical significance
  - P values, CI as noted previously
  - If SS noted: are results clinically significant?
  - If not SS different:
    - Power
    - Fail safe N



Reviews: Major Points

- Validity traps to avoid
  - Assertions based on DOEs -- avoid perpetuating medical gossip
  - Unassessed validity -- Personal experience unreliable as a basis for therapeutic interventions
- Missing pieces -- Quality of the review varies inversely with the expertness of the writer
- Failure to identify level of evidence

Validating Review Articles

Let's Try

- Group exercise applying review article worksheet
- In the patient with OA, is Glucosamine/Chondroitin an effective treatment?

Relevance

- Specific Q/POEMs?
  - Does G/C decrease symptoms in OA?
- Common?
  - Very common
- Change practice?
  - For some, possibly

Finding studies: search comprehensive and clear?

- Terms given, seem appropriate & comprehensive
- Databases searched: CCTR, Medline, bibliography check
- Attempt at unpublished studies: Contacted content experts, study authors, manufacturers

- *Seems quite comprehensive, clearly outlined*

Finding studies: inclusion criteria? generalizable?

- Population: knee or hip OA
- Intervention: glucosamine or chondroitin
- Outcome: hierarchy of outcome measures (POEM focused)
- Design: randomized, placebo-controlled trials

- *Generally looks appropriate and applicable to FP population*

Finding studies: selection process?

- Independently done by two authors
- Any possibly relevant study pulled
- Full inclusion criteria reapplied to full article

Validity of included studies: criteria appropriate?

- Quality Scores (blinding, randomization, w/drawals)
- Noted concealed allocation

- *Generally appropriate criteria*

Validity of included studies:
independent assessment? blinded?

- Done independently by 2 authors
- ? Blinded to title, institution, author, results
- Adjudication process when disagreements
- German article translated

- *Seems to be valid process; better if blinded*

Validity of included studies: trials were valid?

- Table 2 summary; Quality scores 12.3%-55.4%
- Biggest concerns are inadequate allocation concealment and intention-to-treat

- *If studies did not adequately conceal assignment, then results may be overestimate*

Analyzing the data: statistical homogeneity?

- Tests for heterogeneity nonsignificant after removal of 1 outlier trial

Analyzing the data: qualitative homogeneity?

- Population: patients with knee or hip OA
- Intervention: different meds and routes;
- Outcomes: outcomes measured by different methods--combined using “standardized mean difference”

Analyzing the data: publication bias?

- Funnel plot shows asymmetry = relative absence of trials with small numbers or small/null treatment effects

- Publication bias could contribute to overestimation

Interpreting the results: statistical difference?

- Moderate to large effect size
- Quality issues and publication bias

What will you do with the results?